

Figure 1

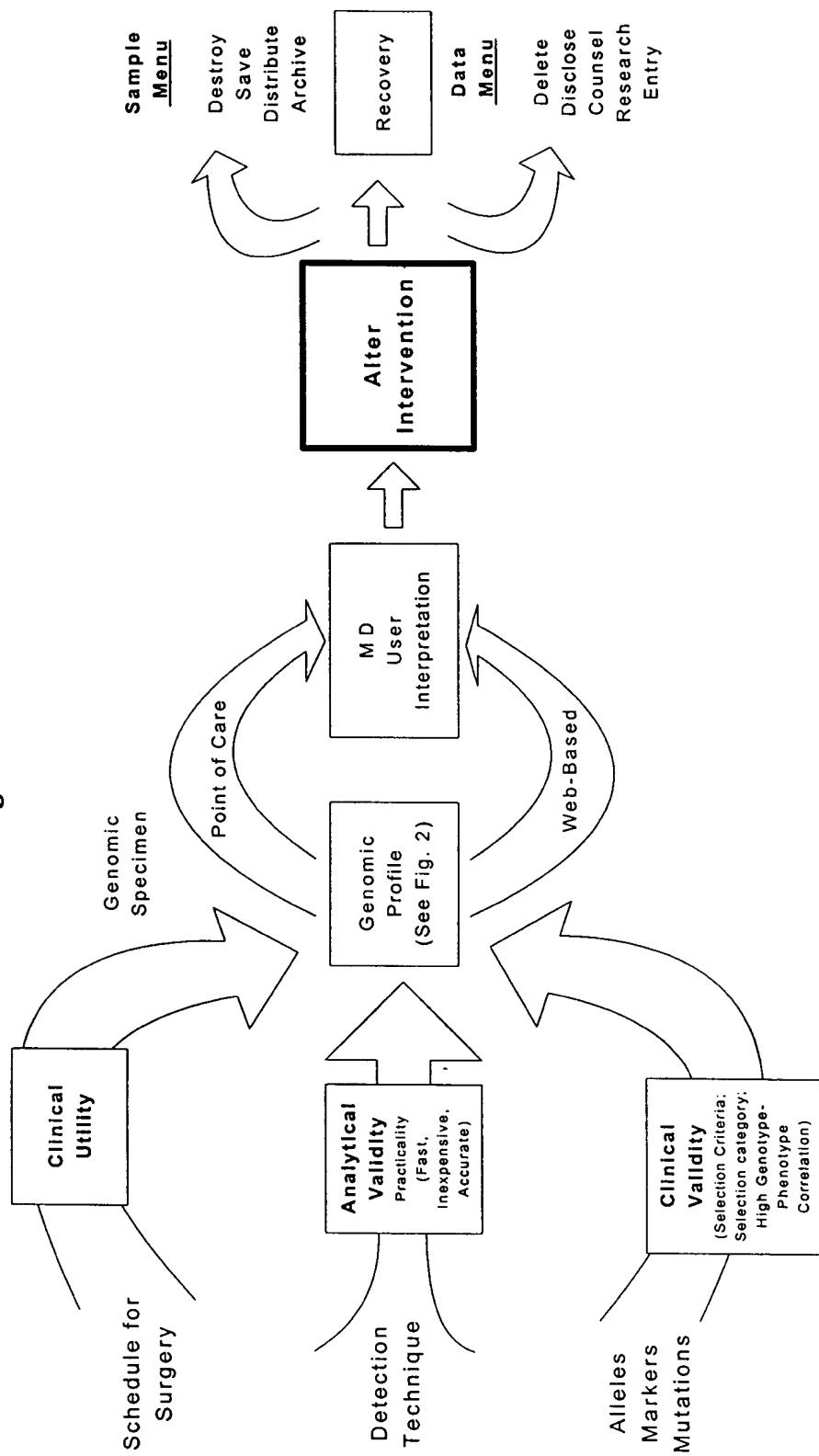


Figure 2

Genomic Profile

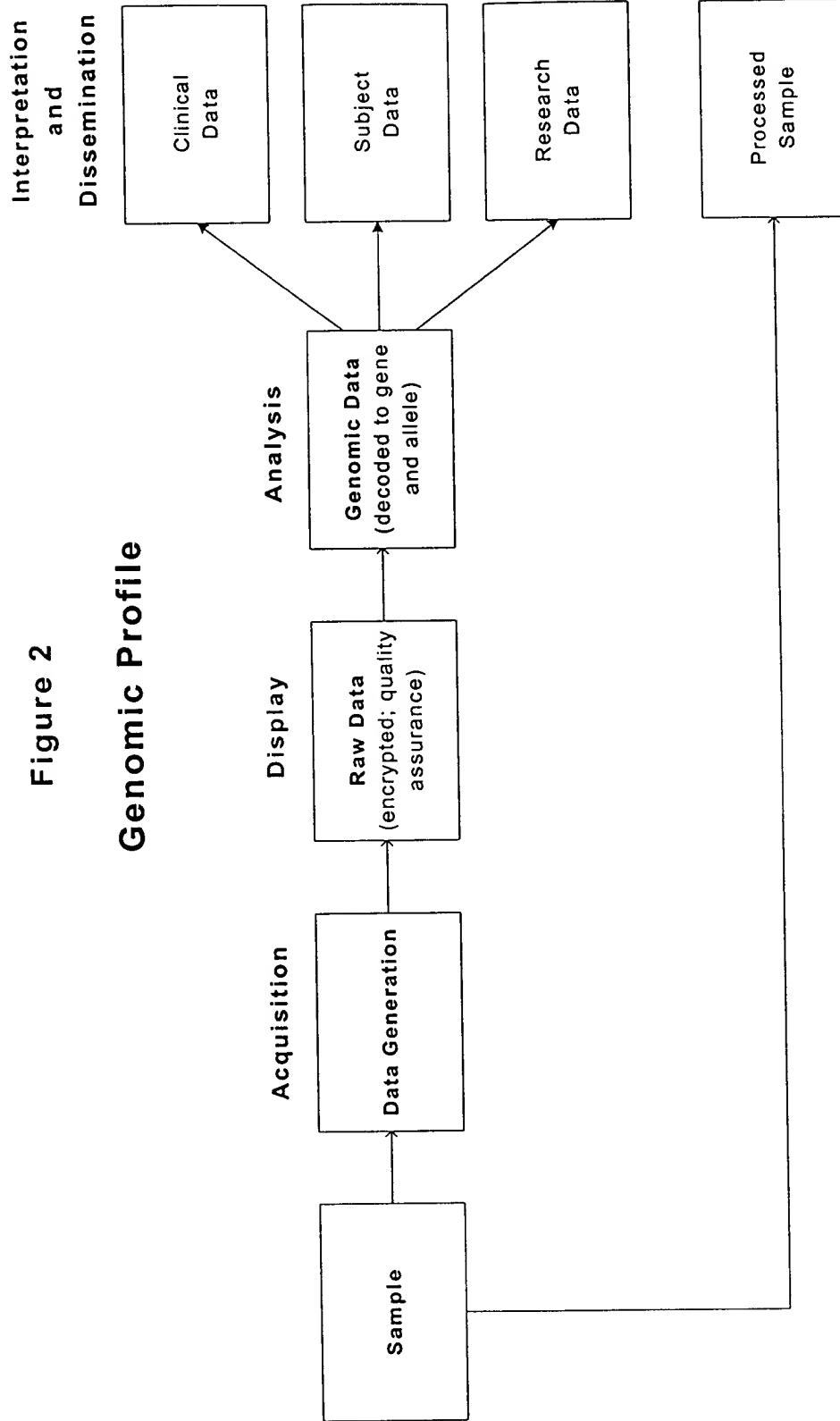


Figure 3

How genomic profiling fits into the flow of information in the perioperative interval

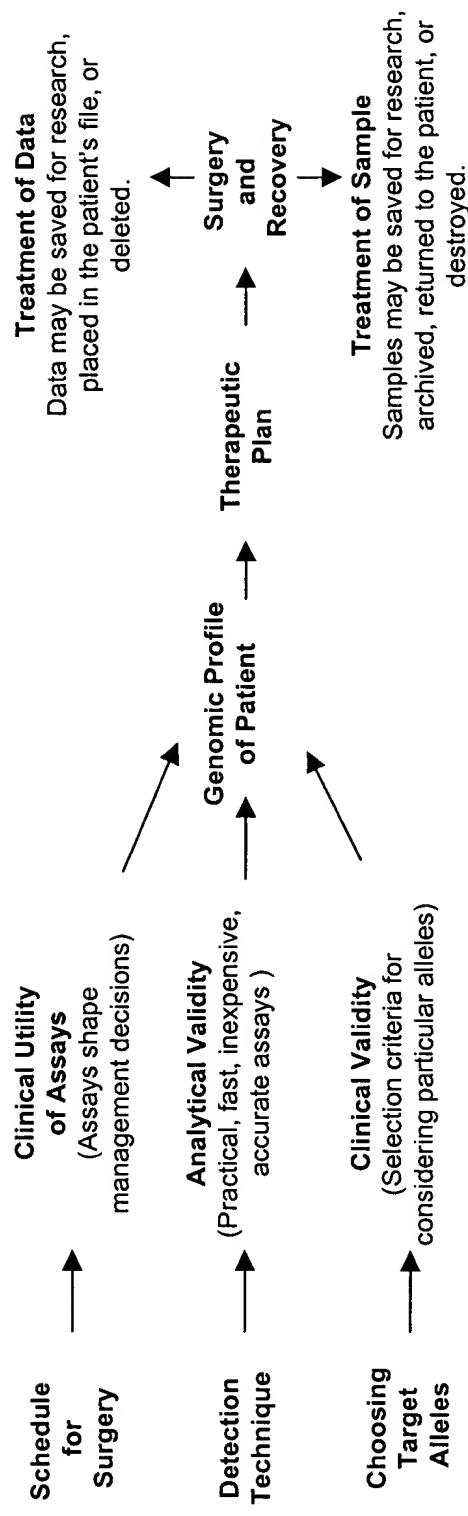


Figure 4
Allele Panel

Gene	Polymorphism	Incidence	Complication	Contra-indicated intervention	Indicated Intervention
BChE	A209G G1615A	0.05%/4%* ("atypical allele") 1.3%/22%* ("K-variant")	prolonged apnea with succinylcholine	succinylcholine, mivacurium	use intermediate duration non-depolarizing muscle relaxants
CYP2D6	G1934A deletion A263 deletion T1795 deletion	66%** 17%** 4%** 4%**	inadequate analgesia with codeine; antiarrhythmic; and tricyclic antidepressant toxicity	omit codeine	use NSAIDs, other opioids; monitor plasma levels for drug toxicity; adjust dose, take drug interaction precautions
MTHFR	C677T A1298C A2756G A66G Intron 7 68bp insertion	12%/>30%* new, not known with precision 2%35%* 29%**** 1%/12%*	elevated blood homocysteine levels; thrombosis	nitrous oxide	avoid nitrous oxide; take thrombosis precautions
MS (MTR) MTRR CBS					
FVL	G1691A	6%****	hyper-coagulable state	If known in advance, avoid prolonged immobilization.	take thrombosis precautions
Prothrombin	G20210A	2%****			
RYR1	G6502A G1021A C1840T C6487T G7303A C7373A G3257A	7%*** 6-10%*** 4%*** 4%*** 4%*** 4%*** 4 families	dysrhythmia, rigidity, renal failure, DIC (disseminated intravascular coagulation), death	succinylcholine; volatile anesthetic agents	use nitrous oxide and non-depolarizing muscle relaxants
CACNA1S	G-308A	16%****			
TNF- α	G+252A	65%****	exaggerated inflammatory response	No specific contraindication	tailor immune modulation; detect inflammatory complications early; watch for infection

* homozygote/heterozygote
** of poor metabolizers
*** of manifesting phenotypes
**** allele frequency

Figure 5
Comparison of INVADER Assay with PCR-RFLP for Detection of Allelic Variants

Assay	Gene	Format	Discrepant	Total
Drug Metabolism				
BCHE G1615A, K variant	butyrylcholinesterase	Monoplex	0	145
BCHE A209G, Atypical		Monoplex	0	164
CYP2D6*3	cytochrome P450 2D6	Biplex	0	168
CYP2D6*4		Biplex	3	164
CYP2D6*5		Biplex	not done	176
CYP2D6*6		Biplex	0	163
Thrombosis				
FVL G1691A	Factor V	Monoplex	1	132
Prothrombin FII G20210A	Factor II	Monoplex	0	140
Homocysteine Level				
MTHFR C677T	methylene tetrahydrofolate reductase	Monoplex	0	145
MTHFR A1298C		Monoplex	0	150
CBS ins68	cystathione beta synthase	Monoplex	0	158
MTR (MS) A2756G	methionine synthase	Monoplex	0	147
MTRR A66G	methionine synthase reductase	Monoplex	2	150
Inflammation				
TNF alpha -308	tumor necrosis factor alpha	Monoplex	2	163
TNFbeta +252	tumor necrosis factor beta	Monoplex	0	163
Total (excluding 2D6*5)			8	2152
Concordance (unresolved)				99.63%